Remarks/Arguments

Claims 23-34, 37-39, 42-43 and 45-49 are currently pending in the instant application. Claims 44 and 50-53 have been withdrawn for being drawn to a non-elected invention and claims 35-36 and 40-41 have been canceled. Applicants have amended claims 28, 34 and 37-39.

Applicants acknowledge the deficiencies of the IDS filed on January 21, 2005 and will be submitting a revised IDS shortly.

Specification

The Examiner has objected to the abstract because it was not submitted on a separate sheet of paper. Applicant has re-submitted the abstract on page 2.

The Examiner has objected to the use of the following trademarks: Cremophor EL, Nikkol HCO-60, Bradosol, Germal II, Purite, Polyquart, Dequest, Cavamax, and Cavasol. As requested by the Examiner, Applicants have amended the specification to capitalize said marks. Applicant respectfully submits that each mark is also accompanied by the generic terminology for the substance identified by each mark.

35 U.S.C. §112 First Paragraph

The Examiner has rejected claims 28-43 and 47 under 35 U.S.C. §112 first paragraph as failing to comply with the written description requirement. Specifically, the Examiner objects to the use of the term "staurosporine derivatives". Applicants respectfully disagree. Applicants have disclosed the chemical structure of staurosporine (*see* ¶[0053] formula (I)) and the two types of derivatives, namely a hydrocarbyl radical or an acyl radical or the ophthalmically acceptable salt thereof. Applicants further go on to identify the possible hydrocarbyl radicals and acyclic hydrocarbyl radicals at ¶¶[0054] and [0055] respectively. Applicants have thus complied with the requirement that the specification describe a sufficient number of representative species that encompass the genus. Although the Examiner alleges that there is "no readily apparent combination of identifying characteristics" Applicants submit that the species each fall into two types of groups, (1) hydrocarbyl radicals and (2) acyclic hydrocarbyl radicals. Applicants further submit that the level of skill in the art is high as we are dealing with drug formulations and Applicants have submitted both the chemical structure for staurosporine and identified with particularity the types of derivatives which would be covered by the claims. Accordingly, Applicants respectfully submit that the claim complies with the written description requirement.

35 U.S.C. §112 Second Paragraph

The Examiner has rejected claims 28-43 and 45-49 under 35 U.S.C. §112 second paragraph as failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner has specifically identified deficiencies with claims 28, 34, 38, 39, 41, and 43. Claim 41 has been canceled.

For claim 28 the Examiner objects to the phrase "semisolid ophthalmic composition". Applicants respectfully submit that as this phrase is located in the preamble of the claim it does not constitute a claim limitation and therefore it is irrelevant whether the claim "provides a means for determining what state of matter would qualify as semisolid."

For claim 34, Applicants have amended the claim to identify that the "parts by weight" refer to the ophthalmic base.

For claims 38-39, Applicants have amended the claim to provide a proper antecedent basis for the claim limitation.

For claim 43, Applicant respectfully submits that the term derivative is commonly understood and used in the art and that the ample identification of possible derivatives contained in ¶¶ [0053]-[0061] are more than sufficient to comply with Applicants' obligation to "particularly point out and distinctly claim" that which Applicants regard as their invention.

35 U.S.C. §102

The Examiner has rejected claims 28-33, 35 and 42 under 35 U.S.C. §102(e) as being anticipated by Chen (U.S. Patent No. 6,579,901) as evidenced by Nobile (U.S. Patent No. 3,134,718). The Examiner has further rejected claims 28-33, 42 and 47 under 35 U.S.C. §102(b) as being anticipated by Sallmann (U.S. Patent No. 6,107,343).

Neither Chen nor Sallmann disclose an ophthalmic composition comprising an ophthalmic drug, an ointment base and a poly(ethylene-glycol). Accordingly, in view of the amendment to claim 28, Applicant respectfully requests withdrawal of these rejections.

35 U.S.C. §103

The Examiner has rejected claims 28-33, 35-42 and 47 under 35 U.S.C. §103(a) as being obvious over Sallmann. The Examiner alleges that Sallmann teaches an eye ointment containing phenylethyl alcohol as a preservative, cetylstearyl alcohol, liquid paraffin, white petrolatum, and wool fat and that Sallmann further teaches that solubilizers such as polyethylene glycols can be included. The Examiner alleges that it would have been obvious to select various combinations of the disclosed solubilizers and fillers from within Sallmann to arrive at compositions "yielding no more than one would expect from such an arrangement." Applicants respectfully disagree.

Sallmann does not disclose the specific combination of features claimed in the instant invention. Rather, poly(ethylene-glycol) is merely disclosed as an optional ingredient among a laundry list of possible ingredients found at c.4, ll.4-11, 23-62. Mixing and matching the dozens

of ingredients would lead to thousands of possible combinations. Yet there is nothing in Sallmann which would motivate one to select the poly(ethylene-glycol) from the plethora of possible ingredients and combine it with an ophthalmic drug and an ointment base. Moreover, there is nothing in Sallmann which would lead one of ordinary skill in the art to anticipate that the claimed invention would have the benefit of being effective and well tolerated when administered to the eye. (*See* ¶¶[00134]-[0141] of the instant application).

The Examienr has further rejected claims 28-33, 35-43, and 45-48 under 35 U.S.C. §103(a) as being obvious over Sallmann in view of Caravatti (U.S. Patent No. 5,093,330). The Examiner admits that Sallmann does not specify inclusion of staurosporine derivatives in the disclosed ophthalmic compositions. The Examiner alleges that Caravatti discloses staurosporine derivatives, specifically midostaurin, in compositions for the treatment of diseases modulated by protein kinase C, including use as an immunomodulator or anti-inflammatory. In the Examiner's view it would have been obvious to employ the anti-inflammatory drugs disclosed in Caravatti in the eye ointments of Sallmann because said eye ointments could be used to treat ocular inflammatory disorders. Applicants respectfully disagree.

Caravatti makes no mention of any possible uses staurosporine derivatives for ophthalmic use. Rather, it discloses them for "tumor-inhibiting, inflammation-inhibiting, immunomodulating, and antibacterial use, and also as preparations for combating arteriosclerosis, diseases of the cardiovascular system and of the central nervous system." (Caravatti at c.2, ll. 42-45). As the eye is a particularly sensitive organ it would not have been obvious to simply apply the compounds disclosed in Caravatti to they eye without potentially severe adverse consequences. The mere fact that Caravatti discloses that staurosporine derivatives may possess anti-inflammatory properties is not sufficient motivation for one of ordinary skill in the art to employ it in an ophthalmic composition with any likelihood of achieving a successful formulation. The fact that the formulations of Sallmann could be used to treat ocular inflammatory disorders with other drugs would not lead one of ordinary skill in the art to believe that the compounds disclosed in Caravatti would be either efficacious or well tolerated when administered in combination with such a formulation. As one of ordinary skill in the art would be neither motivated to make such a combination nor have any likelihood of a successful outcome, Applicants respectfully submit that the claimed invention is not obvious in view of this combination of references.

The Examiner has further rejected claims 28-33, 35-43, and 45-449 under 35 U.S.C. §103(a) as being obvious over Sallmann in view of Caravatti.

As discussed previously, one of ordinary skill in the art would not be motivated to combine the staurosporine derivatives of Caravatti with the formulations of Sallman. Accordingly, claim 49 would likewise be non-obvious.

The Examiner has rejected claims 28-33 35-39, 42 and 47 under 35 U.S.C. §103(a) as being obvious over Chen in view of Oduro (U.S. Patent No. 4,524,075) in further view of Ding

(Shulin Ding, *Recent Developments in Ophthalmic Drug Delivery*, PSTT 328 (November 1998)). The Examiner alleges that Chen teaches ophthalmic compositions comprising tacrolimus, anhydrous lanolin, yellow Vaseline, and poxyoxyethylated castor oil or tacrolimus, anhydrous lanolin, liquid paraffin, yellow Vaseline, and HCO60. The Examiner admits that Chen fails to teach polyethylene glycols. The Examiner next alleges that Oduro describes the use of polyethylene glycol in the formulation of eye ointments. The Examiner next alleges that Ding teaches that viscosity enhancers are commonly used in topical ophthalmic compositions. In the Examiner's view it would have been obvious to include a preservative and polyethylene glycol viscosity enhancer in the composition of Chen. Applicants respectfully disagree.

Oduro teaches the use of polyethylene glycol for the specific purpose of stabilizing pseudomonic acid. (Oduro at c.1, ll.14-16). Therefore, the teaching of this reference cannot be used as a motivation to modify different compositions which lack pseudomonic acid, i.e. those of Chen. Based on only the knowledge at the time of invention and without the benefit of hindsight, there would be no motivation for one of skill in the art to select the polyethylene glycol of Oduro and employ it in the formulations of Chen. Accordingly, absent the impermissible use of hindsight, Applicants' invention is non-obvious in view of this combination of references.

The Examiner has rejected claims 40-14 under 35 U.S.C. §103(a) as being obvious over Chen in view of Camborde (U.S. Patent No. 6,015,797). Applicants have canceled these claims rendering this rejection moot.

The Examiner has rejected claims 43, 45 and 46 under 35 U.S.C. §103(a) as being obvious over Chen in view of Caravatti in further view of Aiello (U.S. Patent No. 6,114,320). The Examiner alleges that Chen describes ophthalmic compositions containing tacrolimus, anhydrous lanolin, vaseline and polyoxyethylated castor oil or tacrolimus, anhydrous lanolin liquid paraffin, vaseline and HCO60. The Examiner next alleges that Caravatti describes the use of staurosporine derivatives. Lastly the Examiner alleges that Aiello describes the use of protein kinase C inhibitors for the treatment of ocular vascular disorders. The Examiner alleges that it would have been obvious for one of ordinary skill in the art to combine staurosporine derivatives with the composition of Chen. As the composition of Chen does not include poly(ethylene-glycol) Applicants respectfully submit that claims 43, 45, and 46 are not obvious in view of the cited prior art.

As Applicants have demonstrated that the prior art combinations cited by the Examiner would not lead one of ordinary skill in the art to the instantly claimed invention, Applicants respectfully request withdrawal of the obviousness rejections and speedy allowance of the application.

Respectfully submitted,

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